Citation:

Djousse L, Gaziano JM. Breakfast cereals and risk of heart failure in the Physicians Health Study I. *Arch Intern Med.* 2007; 167(19): 2,080-2,085.

PubMed ID: 17954802

Study Design:

Prospective Cohort Study

Class:

B - Click here for explanation of classification scheme.

Research Design and Implementation Rating:

NEUTRAL: See Research Design and Implementation Criteria Checklist below.

Research Purpose:

- To prospectively examine whether a higher consumption of total breakfast cereals was associated with a lower risk of heart failure among US male physicians
- Since some of the nutrients are lost or added in refined cereals, to examine whether a higher intake of whole grain, as well as refined breakfast cereals was associated with a lower incidence of heart failure in this population.

Inclusion Criteria:

US male physicians participating in the Physicians Health Study I.

Exclusion Criteria:

Subjects missing information on baseline breakfast cereals, prevalent heart failure or missing covariates.

Description of Study Protocol:

Recruitment

- The study used data from a previously reported randomized trial among US male physicians, the Physician's Health Study I
- In 1981, 261,248 US male physicians were invited to participate in the trial
- After exclusions, 33,223 participants were enrolled in an 18-week run-in-period
- Following run-in, 22,071 subjects were randomized to regimens of low-dose aspirin, beta carotene, both agents or placebo
- For the current project, 695 participants were excluded for missing information
- 21,376 individuals with complete data are included in the analysis.

Design

Prospective cohort study.

Statistical Analysis

- Since there was good correlation between reported breakfast cereals at baseline and at 18 weeks, reported consumption at 18 weeks was substituted for missing values at baseline in 756 individuals
- Within each breakfast cereal group, the incidence rate of heart failure was calculated by dividing the number of heart failure cases by the corresponding person-time
- Cox proportional hazard models were used to compute multivariable adjusted hazard ratios with corresponding 95% confidence intervals (95% CI) across categories of cereal intake
- The fully adjusted model included age, smoking status, alcohol consumption, vegetable consumption, use of multivitamins, physical activity, history of atrial fibrillation, left ventricular hypertrophy and valvular heart disease.

Data Collection Summary:

Timing of Measurements

- Measurements made over an average follow-up of 19.6 years
- Questionnaire mailed to each participant every six months during the first year, annually thereafter
- Cereal consumption obtained at baseline, 18 weeks, and 24, 48, 72, 96 and 120 months after randomization.

Dependent Variables

Incident of heart failure ascertained through annual follow-up questionnaires and validated using Framingham criteria.

Independent Variables

- Consumption of cold breakfast cereals estimated using semi-quantitative food-frequency questionnaire (FFQ)
- Brand of cereals consumed resulted in classification of whole grain or refined grain
- Breakfast cereals containing at least 25% whole grain or bran by weight were classified as whole grain.

Control Variables

- Age
- Smoking (never, past, current)
- Alcohol consumption (less than one, one to four, five to six or seven more drinks per week)
- Vegetable consumption (less than three, three to four, five to six, seven to 13 or 14 or more servings per week)
- Use of multivitamins (never, past, current)
- Exercise (less than one or one or more time per week)
- History or atrial fibrillation, valvular heart disease and left ventricular hypertrophy.

Description of Actual Data Sample:

- *Initial N:*
  - 22,071 subjects were originally randomized to regimens of low-dose aspirin, beta carotene, both agents or placebo
  - 695 participants were excluded for missing information
- *Attrition (final N):* 21,376 participants, all male physicians
- *Age:* Mean age at randomization was 53.7±9.5 years (range 40 to 86 years)
- *Location:* United States.

Summary of Results:

Incidence Rates and Hazard Ratios of Heart Failure by Breakfast Cereal Intake

Cereal Intake, One Cup Servings per Week	Number of Cases	Crude Incidence Rate, Cases per 10,000 Person-Years	Adjusted Hazard Ratio (95% CI)	P-value
Zero	362	26.7	1 (Reference)	<0.001 for trend
One or less	237	24.1	0.92 (0.78 to 1.09)	
Two to six	230	22.2	0.79 (0.67 to 0.93)	
Seven or more	189	23.3	0.71 (0.60 to 0.85)	

Other Findings

- During an average follow-up of 19.6 years, 1,018 incident cases of heart failure occurred
- Frequent consumption of breakfast cereals was associated with:
  - Older age
  - Higher consumption of vegetables
  - Higher proportion of current drinkers, those engaging in physical activity at least once a week and users of multivitamins
  - Lower proportion of current smokers
  - Lower prevalence of hypertension
- However, the association was limited to the intake of whole-grain cereals (P<0.001 for trend), but not refined cereals (P=0.70 for trend).

Author Conclusion:

- Data showed an inverse association between consumption of whole-grain breakfast cereals and incident heart failure. Such association is more likely to be mediated through beneficial effects of whole grains on risk factors of heart failure such as hypertension, myocardial infarction, diabetes mellitus and obesity
- If confirmed in other studies, a higher intake of whole grains along with other preventive measures could help lower the risk of heart failure.

Reviewer Comments:

- *Almost 20 years of follow-up and large sample size*
- *Only cold cereal, not hot cereals, were studied*
- *Only 25% whole grain or bran needed to be classified as whole grain cereal*
- *Authors note the following limitations:*
  - *Did not collect data to distinguish heart failure with and without preserved left ventricular function*
  - *Were unable to control for total energy intake and other nutrients in the diet*
  - *Possibility of inaccurate reporting of consumption of breakfast cereals, which might have led to exposure misclassification*
  - *Sample consisted of highly educated male physicians who may have different behaviors than the general population; this may limit the generalizability of the findings*
  - *Given the inter-correlation between cereal consumption and other dietary or lifestyle factors, the data cannot precisely estimate the net contribution of cereal consumption on the observed association.*

Research Design and Implementation Criteria Checklist: Primary Research

Relevance Questions

1.	Would implementing the studied intervention or procedure (if found successful) result in improved outcomes for the patients/clients/population group? (Not Applicable for some epidemiological studies)	N/A
2.	Did the authors study an outcome (dependent variable) or topic that the patients/clients/population group would care about?	Yes
3.	Is the focus of the intervention or procedure (independent variable) or topic of study a common issue of concern to nutrition or dietetics practice?	Yes
4.	Is the intervention or procedure feasible? (NA for some epidemiological studies)	N/A

Validity Questions

1.	**Was the research question clearly stated?**	Yes
1.1.	Was (were) the specific intervention(s) or procedure(s) [independent variable(s)] identified?	Yes
1.2.	Was (were) the outcome(s) [dependent variable(s)] clearly indicated?	Yes
1.3.	Were the target population and setting specified?	Yes
2.	**Was the selection of study subjects/patients free from bias?**	???

2.1.	Were inclusion/exclusion criteria specified (e.g., risk, point in disease progression, diagnostic or prognosis criteria), and with sufficient detail and without omitting criteria critical to the study?	No
2.2.	Were criteria applied equally to all study groups?	???
2.3.	Were health, demographics, and other characteristics of subjects described?	Yes
2.4.	Were the subjects/patients a representative sample of the relevant population?	???
3.	**Were study groups comparable?**	Yes
3.1.	Was the method of assigning subjects/patients to groups described and unbiased? (Method of randomization identified if RCT)	N/A
3.2.	Were distribution of disease status, prognostic factors, and other factors (e.g., demographics) similar across study groups at baseline?	N/A
3.3.	Were concurrent controls used? (Concurrent preferred over historical controls.)	N/A
3.4.	If cohort study or cross-sectional study, were groups comparable on important confounding factors and/or were preexisting differences accounted for by using appropriate adjustments in statistical analysis?	Yes
3.5.	If case control or cross-sectional study, were potential confounding factors comparable for cases and controls? (If case series or trial with subjects serving as own control, this criterion is not applicable. Criterion may not be applicable in some cross-sectional studies.)	N/A
3.6.	If diagnostic test, was there an independent blind comparison with an appropriate reference standard (e.g., "gold standard")?	N/A
4.	**Was method of handling withdrawals described?**	Yes
4.1.	Were follow-up methods described and the same for all groups?	Yes
4.2.	Was the number, characteristics of withdrawals (i.e., dropouts, lost to follow up, attrition rate) and/or response rate (cross-sectional studies) described for each group? (Follow up goal for a strong study is 80%.)	Yes
4.3.	Were all enrolled subjects/patients (in the original sample) accounted for?	Yes
4.4.	Were reasons for withdrawals similar across groups?	N/A
4.5.	If diagnostic test, was decision to perform reference test not dependent on results of test under study?	N/A
5.	**Was blinding used to prevent introduction of bias?**	N/A

5.1.	In intervention study, were subjects, clinicians/practitioners, and investigators blinded to treatment group, as appropriate?	N/A
5.2.	Were data collectors blinded for outcomes assessment? (If outcome is measured using an objective test, such as a lab value, this criterion is assumed to be met.)	N/A
5.3.	In cohort study or cross-sectional study, were measurements of outcomes and risk factors blinded?	N/A
5.4.	In case control study, was case definition explicit and case ascertainment not influenced by exposure status?	N/A
5.5.	In diagnostic study, were test results blinded to patient history and other test results?	N/A
6.	**Were intervention/therapeutic regimens/exposure factor or procedure and any comparison(s) described in detail? Were interveningfactors described?**	Yes
6.1.	In RCT or other intervention trial, were protocols described for all regimens studied?	N/A
6.2.	In observational study, were interventions, study settings, and clinicians/provider described?	Yes
6.3.	Was the intensity and duration of the intervention or exposure factor sufficient to produce a meaningful effect?	N/A
6.4.	Was the amount of exposure and, if relevant, subject/patient compliance measured?	N/A
6.5.	Were co-interventions (e.g., ancillary treatments, other therapies) described?	N/A
6.6.	Were extra or unplanned treatments described?	N/A
6.7.	Was the information for 6.4, 6.5, and 6.6 assessed the same way for all groups?	N/A
6.8.	In diagnostic study, were details of test administration and replication sufficient?	N/A
7.	**Were outcomes clearly defined and the measurements valid and reliable?**	???
7.1.	Were primary and secondary endpoints described and relevant to the question?	Yes
7.2.	Were nutrition measures appropriate to question and outcomes of concern?	Yes
7.3.	Was the period of follow-up long enough for important outcome(s) to occur?	Yes
7.4.	Were the observations and measurements based on standard, valid, and reliable data collection instruments/tests/procedures?	???
7.5.	Was the measurement of effect at an appropriate level of precision?	???
7.6.	Were other factors accounted for (measured) that could affect outcomes?	No

	7.7.	Were the measurements conducted consistently across groups?	Yes
8.	**Was the statistical analysis appropriate for the study design and type of outcome indicators?**		Yes
	8.1.	Were statistical analyses adequately described and the results reported appropriately?	Yes
	8.2.	Were correct statistical tests used and assumptions of test not violated?	Yes
	8.3.	Were statistics reported with levels of significance and/or confidence intervals?	Yes
	8.4.	Was "intent to treat" analysis of outcomes done (and as appropriate, was there an analysis of outcomes for those maximally exposed or a dose-response analysis)?	N/A
	8.5.	Were adequate adjustments made for effects of confounding factors that might have affected the outcomes (e.g., multivariate analyses)?	Yes
	8.6.	Was clinical significance as well as statistical significance reported?	Yes
	8.7.	If negative findings, was a power calculation reported to address type 2 error?	N/A
9.	**Are conclusions supported by results with biases and limitations taken into consideration?**		Yes
	9.1.	Is there a discussion of findings?	Yes
	9.2.	Are biases and study limitations identified and discussed?	Yes
10.	**Is bias due to study's funding or sponsorship unlikely?**		Yes
	10.1.	Were sources of funding and investigators' affiliations described?	Yes
	10.2.	Was the study free from apparent conflict of interest?	Yes